-- Figure 1 shows mutant-specific oligonucleotide primers *Bet v 1* sense (SEQ ID NO: 97), *Bet v 1* non-sense (SEQ ID NO: 98), sense primer (SEQ ID NO: 99) and non-sense primer (SEQ ID NO: 100) used for *Bet v 1* mutant number 1. Mutated nucleotides are underlined.

Figure 2 shows two generally applicable primers 183Bv (SEQ ID NO: 101) and 200Bv (SEQ ID NO: 116) used for all mutants and specific mutagenesis primers 184Bv (SEQ ID NO: 99), 185Bv (SEQ ID NO: 100), 186Bv (SEQ ID NO: 102), 187Bv (SEQ ID NO: 103), 188Bv (SEQ ID NO: 104), 189Bv (SEQ ID NO: 105), 190Bv (SEQ ID NO: 106), 191Bv (SEQ ID NO: 107), 192Bv (SEQ ID NO: 108), 193Bv (SEQ ID NO: 109), 194Bv (SEQ ID NO: 110), 195Bv (SEQ ID NO: 111), 196Bv (SEQ ID NO: 112), 197Bv (SEQ ID NO: 113), 198Bv (SEQ ID NO: 114), 199Bv (SEQ ID NO: 115).

Figure 3 shows the DNA (SEQ ID NO: 91) and amino acid (SEQ ID NO: 92) sequences of the naturally occurring allergen Bet v 1 as well as a number of Bet v 1 mutations.

Figure 4 shows the inhibition of the binding of biotinylated recombinant Bet v 1 to serum IgE from a pool of allergic patients by non-biotinylated Bet v 1 and by Bet v 1 Glu45Ser mutant.

Figure 5 shows the inhibition of the binding of biotinylated recombinant Bet v 1 to serum IgE from a pool of allergic patients by non-biotinylated Bet v 1 and by Bet v 1 mutant Asn28Thr+Lys32Gln.

Figure 6 shows the inhibition of the binding of biotinylated recombinant Bet v 1 to serum IgE from a pool of allergic patients by non-biotinylated Bet v 1 and by Bet v 1 Pro108Gly mutant.

Figure 7 shows the inhibition of the binding of biotinylated recombinant Bet v 1 to serum IgE from a pool of allergic patients by non-biotinylated Bet v 1 and by Bet v 1 Glu60Ser mutant.

Figure 8 shows the CD spectra (10 mM Na_2HPO_4/NaH_2PO_4; 0.02%Na_3N_3) of recombinant and Triple-patch mutant, recorded at close to equal concentrations.

Figure 9 shows the inhibition of the binding of biotinylated recombinant Bet v 1 to serum IgE from a pool of allergic patients by non-biotinylated Bet v 1 and by Bet v 1 Triple-patch mutant.

Figure 10A-B shows solvent accessibility of individually aligned antigen 5 residues and alignment of Vespula antigen 5 sequences (A) and the molecular surface of antigen 5 with conserved areas among Vespula antigen 5:s (B).

Figure 11A-B shows the sequence of the mutant specifice primers used for Ves v 5 mutants. Ves v 5 mutant 1 (K72A) primers in (A) were Ves v sense (SEQ ID NO: 127), Ves v 5 non-sense (SEQ ID NO: 128), sense primer (SEQ ID NO: 129) and non-sense primer (SEQ ID NO: 130). Ves v 5 mutant 2 (Y96A) primers in (B) were were Ves v sense (SEQ ID NO: 131), Ves v 5 non-sense (SEQ ID NO: 132), sense primer (SEQ ID NO: 133) and non-sense primer (SEQ ID NO: 134).

Figure 12 shows oligonucleotide primers for site directed mutagenesis of Ves v 5 with [two] generally applicable primers Xho I start (SEQ ID NO: 215) and CT-pPICZαA (SEQ ID NO: 135) used for all mutants and specific primers K72As (SEQ ID NO: 129), K72Aa (SEQ ID NO: 130), Y96As (SEQ ID NO: 133) and Y96Aa (SEQ ID NO: 134).

Figure 13 shows the DNA (SEQ ID NO: 136) and amino acid (SEQ ID NO: 117) sequences of the naturally occurring allergen Ves v 5 as well as two Ves v 5 mutations.

Figure 14 shows the inhibition of the binding of biotinylated recombinant Ves v 5 to serum IgE from a pool of allergic patients by non-biotinylated Ves v 5 and by Ves v 5 Lys72Ala mutant.

Figure 15A-B depicts the effect of point mutations in dominating IgE epitopes in a model with 3 epitopes, showing of the reaction between an allergen and mast cells by IgE cross-linking.

Figure 16A-B shows the DNA (A) (SEQ ID NO: 137; accession no. P49278 SWISSPROT) and amino acid (B) (SEQ ID NO: 138; accession no. P49278 SWISSPROT; signal peptide 1-17) sequences of the naturally occurring allergen Der p 2.

Figure 17 shows schematically the primers used to create the mutations. (I) shows the sense and antisense primers. (II) shows the final recombinant protein harbouring mutations at the indicated positions. Lines represent DNA sequences; numbers in parentheses above lines represent sense oligonucleotide primers (1), (3), (5), (7), (9) and (11); numbers in parentheses below lines represent anti-sense nucleotide primers (2), (4) (6), (8), (10) and (12); notation is X (position) Y represents mutations; (1) represents the sense oligonucleotide primer accommodating the proteins N-terminus; and (12) represents the anti-sense oligonucleotide accommodating the protein C-terminus.

Figure 18A-B shows an illustration of the construction of (A) Bet v 1 mutant (2628) and (B) Bet v 1 mutant (2637).

Figure 19A-B shows introduced point mutations at the surface of (A) Bet v 1 (2628) and (B) Bet v 1 (2637) showing backbone + amino acids 95-100% conserved among *Fagales* (grey) and introduced point mutations (black). In mutant Bet v 1 (2628), five primary mutations were introduced in one half of Bet v 1 leaving the other half unaltered. In mutant Bet v 1 (2637), five primary and three secondary mutations were introduced in the other half, leaving the first half unaltered.

Figure 20 shows the circular dichroism (CD) spectra of recombinant Bet v 1.2801 (wild type) and the Bet v 1 (2637) mutant recorded at nearly identical concentrations.

Figure 21 shows the inhibition of the binding of biotinylated recombinant Bet v 1.2801 (wild type) to serum IgE from a pool of allergic patients by non-biotinylated Bet v 1.2801 and by Bet v 1 (2628), Bet v 1 (2637), and a 1:1 mix of Bet v 1 (2628) and Bet v1 (2637).

Figure 22 shows histamine release in human basophil cells (donor MCDS) of Bet v 1.2801 (wild type), Bet v 1 (2628), and Bet v 1 (2637).

Figure 23 shows histamine release in human basophil cells (donor MDH) of Bet v 1.2801 (wild type), Bet v 1 (2628), and Bet v 1 (2637).

Figure 24 shows point mutations at the surface of Bet v 1 (2744) showing back bone + amino acid residues 95-100% conserved among *Fagales* (grey) and point mutations (black).

Figure 25 shows point mutations at the surface of Bet v 1 (2753) showing back bone + amino acid residues 95-100% conserved among *Fagales* (grey) and point mutations (black).

Figure 26 shows point mutations at the surface of Bet v 1 (2744) and Bet v 1 (2753) showing molecular surface amino acids 95-100% conserved among *Fagales* (grey); mutations (Y5V, K134E), (E42S, E45S), (N78K, K103V), K123I and (D156H, +160N) (black); and mutations (N28T, K32Q), K65N, (E96L, K97S), (P108G, D109N), (D125Y, E127S) and R145E (white).

Figure 27 shows circular dichroism (CD) spectra of Bet v 1.2801 (wild type) and Bet v 1 (2744), recorded at nearly equal concentrations.

Figure 28 shows histamine release in human basophil cells (donor MK) of Bet v 1.2801 (wild type), and mutant Bet v 1 (2744).

Figure 29A-D shows histamine release in human basophil cells of Bet v 1.2801 (wild type), and mutant Bet v 1 (2744) for donors MJ (A), MH (B), CJB (C) and MCDS (D).

Figure 30 shows point mutations at the surface of Bet v 1 (2733) showing back bone + amino acid residues 95-100% conserved among Fagales (grey) and point mutations (black) Y5V, N28T, K32Q, E45S, K65N, N78K, K97S, K103V, P108G, K134E, R145E, D156H and + 160N.

Figure 31 shows primers used for site-directed mutagenesis of Der p 2, OB43 (SEQ ID NO: 155), OB28 (SEQ ID NO: 158), OB44 (SEQ ID NO: 157), OB46 (SEQ ID NO: 159), OB47 (SEQ ID NO: 161), OB48 (SEQ ID NO: 162), OB49 (SEQ ID NO: 163) and OB50 (SEQ ID NO: 165).

Figure 32 shows a sequence alignment of Der p 2 with other group 2 house dust mite allergens.

Figure 33 shows surface contours of Der p 2 from four different angles.

Figure 34 shows surface contours of a Der p 2 mutant from four different angles.

Figure 35A-B shows a sequence alignment of Der p 1 with other group 1 house dust mite allergens.

Figure 36 shows surface contours of Der p 1 from four different angles.

Figure 37 shows surface contours of a Der p 1 mutant from four different angles.

Figure 38A-D shows a sequence alignment of Phl p 5 with other group 5 grass allergens.

Figure 39A-B shows surface contours of Phl p 5 Model A and Model B, respectively, from four different angles.

Figure 40A-B shows surface contours of a Phl p 5 mutant Model A and B, respectively, from four different angles.

Figure 41 shows the Bet v 1-specific proliferation of Peripheral Blood Lymphocytes expressed as Stimulation Index (SI) for various Bet v 1 preparations (patient PBL).

Figures 42-44 show the cytokine profile of T cells stimulated with various Bet v preparations. Figure 42 shows a patient with a Th0 profile, Figure 43 a Th1 profile and Figure 44 a Th2 profile. --

Please amend the paragraph at page 32, lines 8-9 to read as follows:

-- Examples of *Der p 2* mutants according to the present invention are as follows:--

Please amend the paragraph consisting of the last line on page 67 and the first line on page 68 to read as follows:

-- 3-D structure is based on accession number Q05110 (pdb coordinates unpublished). Numbering of Ves v 5 amino acids used in the text conforms with SEQ ID NO: 214. --

Please amend the paragraph bridging pages 82-83 to read as follows:

-- Figure 18A-B shows synthesised oligonucleotide primers and schematically illustrations for the construction of Bet v 1 mutants with five to nine primary mutations. Figure 18A illustrates construction of Bet v 1 (2628) using primers p331pMal c (SEQ ID NO: 139), 189BV (SEQ ID NO: 140), 188BV (SEQ ID NO: 141), 362BVa (SEQ ID NO: 142), 361BVs (SEQ ID NO: 143), 364 BVa (SEQ ID NO: 144), 363BVs (SEQ ID NO: 145), 366BVa (SEQ ID NO: 146), 365BVs (SEQ ID NO: 147) and 332pMal c (SEQ ID NO: 148) and Bet v 1 (2589) as template. Figure 18B illustrates construction of Bet v 1 (2637) using primers 331pMalc (SEQ ID NO: 149), 368BVa (SEQ ID NO: 150), 367BVs (SEQ ID NO: 151), 370BVa (SEQ ID NO: 152), 369BVs (SEQ ID NO: 153) and 372Bva (SEQ ID NO: 154) and Bet v 1 (2571) as template. The mutated amino acids were preferably selected from the group consisting of amino acids that are characterised by being highly solvent exposed and conserved as described in Example 3. The Bet v 1 mutants are the following primary and secondary mutations stated in parenthesis:--

Please amend the paragraph at page 91, lines 6-17 to read as follows:

-- PCR amplified products from first strand cDNA synthesis of *Dermatophagoides pteronyssinus* total RNA was obtained from Dr. Wendy-Anne Smith and Dr. Wayne Thomas (TVW Telethon Institute for Child Health Research, 100 Roberts Rd, Subiaco, Western Australia 6008). During the amplification of the first strand cDNA library, Der p 2 had been selectively amplified using Der p 2 specific primers. PCR fragments were subsequently cloned into the Bam HI site of pUC19 (New England BioLabs). DNA sequencing of Der p 2 was performed using vector specific sense (5'-GGCGATTAAGTTGGGTAACGCCAGGG-3'; SEQ ID NO: 160) and anti-sense (5'-GGAAACAGCTATGACCATGATTACGCC-3'; SEQ ID NO: 164) primers. --

Please amend the paragraph at page 92, lines 1-29 to read as follows:

--The gene encoding Der p 2 (ALK-114) was subsequently inserted into the pGAPZα-A vector (Invitrogen) for secreted expression of Der p 2 in the yeast, *Pichia pastoris*. The gene was amplified using sense primer OB27 (5'- GGAATTCCTCGAGAAAAGA-GATCAAGTCGATGTCAAAGATTGTGCC-3'; SEQ ID NO: 158) and anti-sense primer OB28 (5'-CGTTCTA GACTATTAATCGCGGATTTTAGCATGAGTTGC-3'; SEQ ID NO: 166) corresponding to the amino- and the carboxytermi of the Der p 2 polypeptide, respectively. The primers were extended in the 5'-end to accomodate the restriction sites Xho I and Xba I, respectively. The Xho I restriction site fuses the first codon of Der p 2 in frame with the nucleic acid sequence encoding the KEX2 cleavage site (LYS-ARG) of pGAPZα-A. A single round of PCR amplification was performed in a 100 microliter (μl) volume: 0.1 mg of template ALK-114 DNA, 1 X Expand polymerase buffer (available from Boehringer Mannheim), 0.2 millimolar (mM) each of the four dNTPs, 0.3 micromolar (μM) each of the sense and anti-sense primers and 2.5 Units of Expand polymerase (available from Boehringer Mannheim). The DNA was amplified following 25 cycles of: 95°C for 15 seconds, 45°C for 30 seconds, 72°C for 1 minute, followed by 1 cycle of 72°C for 7 minutes. The resulting 475 base pair ALK-114 PCR fragment was purified using a QIAquick spin purification procedure (available from Qiagen). The purified DNA fragment was then digested with Xho I and Xba I, gel purified and ligated into similarly digested pGAPZα-A. The ligation reaction was trasformed into *E.coli* strain DH5α, resulting in plasmid, pCBo06. --

Please amend the paragraph found at page 93, lines 3-4 to read as follows:

-- SEQ ID NO: 89 corresponds to the nucleic acid sequence of Der p 2 (ALK-114): --

Please amend the paragraph found at page 93, lines 14-15 to read as follows:

-- SEQ ID NO: 90 corresponds to the deduced amino acid sequence of Der p 2 (ALK-114): --

Please amend the two paragraphs found at page 96, lines 8-14 to read as follows:

-- The nucleotide and deduced amino acid sequences of Der p 2-ALK-G clone, which is a wild type isoform, are given in SEQ ID NO: 93 and SEQ ID NO: 94, respectively.

Nucleotide (SEQ ID NO: 93) and deduced amino acid sequence (SEQ ID NO: 94) of Der p 2-ALK-G. --

Please amend the paragraph bridging pages 96-97 to read as follows:

-- Fig. 32 shows a sequence alignment performed at the ExPaSy Molecular Biology Server (http://www.expasy.ch/) using the ClustalW algorithm on a BLAST search using the Der p 2-ALK-G amino acid sequence shown in SEQ ID NO: 94 as input sequence. The alignment includes sequences from house dust mite species, i.e. Der p 2, Der f 2 and Eur m 2. In Fig. 32 amino acid residues identical to amino acids in the same position in the Der p 2-ALK-G protein sequence are highlighted using black letters on grey background. Non-identical amino acids are printed in black on a white background. Sequences aligned are , DERP2-ALK-G (SEQ ID NO: 94), DERP2 CDNA (SEQ ID NO: 90), DERP2-ISO101 (SEQ ID NO: 167), DERP2-ISO102 (SEQ ID NO: 168), DERP2-ISO104 (SEQ ID NO: 169), DERP2-ISO113 (SEQ ID NO: 170), DERP2-ISO120 (SEQ ID NO: 171), 1A9V (SEQ ID NO: 172), DEF2_DERFA (SEQ ID NO: 173), B61241 (SEQ ID NO: 174), 1AHK (SEQ ID NO: 175), A61501 (SEQ ID NO: 176), O96430 (SEQ ID NO: 177) and Q9TZZ2 (SEQ ID NO: 178).--

Please amend the two paragraphs found at page 103, lines 15-20 to read as follows:

-- The nucleotide and deduced amino acid sequences of Der p 1-ALK clone, which is a wild-type isoform, are given in SEQ ID NO: 87 and SEQ ID NO: 88, respectively.

Nucleotide (SEQ ID NO: 87) and deduced amino acid (SEQ ID NO: 88) sequences of Der p 1-ALK.--

Please amend the paragraph found at page 104, lines 14-24 to read as follows:

-- Fig. 35A-B shows a sequence alignment performed at the ExPaSy Molecular Biology Server (http://www.expasy.ch/) using the ClustalW algorithm on a BLAST search using the Der p 1-ALK amino acid sequence shown in SEQ ID NO:88 as input sequence. The alignment includes sequences from house dust mite species, i.e. Der p 1, Der f 1 and Eur m 1. In Fig. 35A-B amino acid residues identical to amino acids in the same position in the Der p 1-ALK protein sequence are highlighted using black letters on grey background. Non-identical amino

acids are printed in black on a white background. Sequences aligned are Der p1 ALK (SEQ ID NO: 88), Der p 1 (SEQ ID NO: 177), Eur m 1.0101 (SEQ ID NO: 180), Eur m 1.0101 (SEQ ID NO: 181), Eur m 1.0102 (SEQ ID NO: 182), Der f 1 (SEQ ID NO: 183), Eur m 1 (SEQ ID NO: 184) and Der f 1 (SEQ ID NO: 185).--

Please amend the two paragraphs found at page 112, lines 3-9 to read as follows:

-- The nucleotide and deduced amino acid sequences of Phl p 5.0103, which is a wild-type isoform, are given in SEQ ID NO: 95 and SEQ ID NO: 96, respectively.

Nucleotide (SEQ ID NO: 95) and deduced amino acid (SEQ ID NO: 96)sequences of Phl p 5.0103.--

Please amend the paragraph found at page 113, lines 1-13 to read as follows:

-- Fig. 38A-D shows a sequence alignment performed at the ExPaSy Molecular Biology Server (http://www.expasy.ch/) using the ClustalW algorithm on a BLAST search using the Phl p 5.0103 amino acid sequence shown in SEQ ID NO: 96 as input sequence. The alignment includes group 5 allergen sequences from grass species, i.e. Phl p 5, Poa p 5, Lol p 5, Hol l 5, Pha a 5, Hor v 9 and Hor v 5. In Fig. 38A-D amino acid residues identical to amino acids in the same position in the Phl p 5.0103 protein sequence are highlighted using black letters on grey background. Non-identical amino acids are printed in black on a white background. Sequences aligned are , Phl p 5.0103 (OB1341) (SEQ ID NO: 186), Phl p 5 (Q40960) (SEQ ID NO: 187), Phl p 5A (Q40962) (SEQ ID NO: 188), Poa p 5 (KBG41) (P22285) (SEQ ID NO: 189), Poa p 5 (KBG60) (P22286) (SEQ ID NO: 190), Phl p 5 (O65319) (SEQ ID NO: 191), Phl p 5 (O65320) (SEQ ID NO: 192), Phl p 5 (O65321) (SEQ ID NO: 193), Phl p 5 (O65318) (SEQ ID NO: 194), Phl p 5 (P93467) (SEQ ID NO: 195), Poa p 5 (KBG31) (P22284) (SEQ ID NO: 196), Lol p 5B (Q40237) (SEQ ID NO: 197), Lol p 5A (Q9XF24) (SEQ ID NO: 198), Lol p 5 C (Q9SC99) (SEQ ID NO: 199), Phl p 5.0206 (OB1343) (SEQ ID NO: 200), Hol I 5 (O23972) (SEQ ID NO: 201), Phl p 5.0207 (OB1344) (SEQ ID NO: 202), Hol I 5B (AAG42255) (SEQ ID NO: 203), Poa p 5 (AAG42254) (SEQ ID NO: 204), Phl p 5.0203 (OB1342) (SEQ ID NO: 205), Phl p 5 (P93466) (SEQ ID NO: 206), Phl p 5B (Q40963) (SEQ ID NO: 207), Phl p 5.0204 (Q9SBE0) (SEQ ID NO: 208), Phl p 5.02 (O23971) (SEQ ID NO: 209), Pha a 5.3 (P56166) (SEQ ID NO: 210), Pha a 5.1 (HAAQ) (SEQ ID NO: 211), Hor v 9 (O04828) (SEQ ID NO: 212) and Hor v 5 (30kDa) (Q39995) (SEQ ID NO: 213).--